

LOOMIS (H.P.)

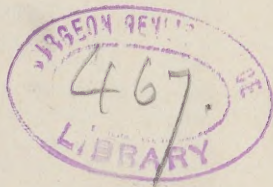
A Study of the Processes which
Result in the Arrest or
Cure of Phthisis

BY

HENRY P. LOOMIS, M.D.

NEW YORK

Reprinted from the MEDICAL RECORD, January 9, 1892



NEW YORK

TROW DIRECTORY, PRINTING AND BOOKBINDING CO.

201-213 EAST TWELFTH STREET

1892

A STUDY OF THE PROCESSES WHICH RESULT IN THE ARREST OR CURE OF PHTHISIS.¹

I HAVE endeavored, in a series of observations extending over the past two years, and by the aid of abundant material which has come to me during my service as Curator at Bellevue Hospital, to obtain some explanation of the following anatomical changes which form a part of the morbid anatomy of pulmonary tuberculosis :

1. In what proportion of cases met with on the autopsy table are found the evidences of cured pulmonary tuberculosis ?

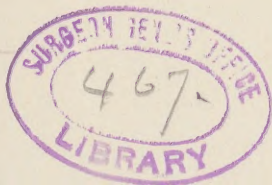
2. What are the gross and microscopical appearances presented by the lungs in these cases, and by what histological changes was the cure effected ?

3. In the healed lungs, are tubercle bacilli still present ?

4. How often are the evidences of localized or general adhesive pleurisy found, and what effect have such pleuritic changes had on the pulmonary structure ?

Anyone who has the opportunity of making a large number of autopsies soon becomes impressed with two facts : First, it is the exception to find perfectly normal lungs, or lungs which are not more or less firmly bound to the chest-wall by old pleuritic adhesions, either localized or general. These adhesions are sometimes so firm and dense that the lungs can only be removed with the costal pleura attached. Secondly, the number of cases where the lungs must at some time have been the seat of

¹ Read before the Section on Practice, New York Academy of Medicine, December 15, 1891.



an active and often extensive tuberculosis, yet at the time of death all traces of active processes have disappeared and the destroyed pulmonary parenchyma been replaced by fibrous tissue.

This tissue generally shows itself at the apex of otherwise normal lungs, as firm, dense, circumscribed masses, which vary in size from a half to two inches in diameter, and have in their centre cheesy or calcareous concretions. Sometimes a small and completely encysted cavity is met with in otherwise healthy lungs. For a long time, I have been convinced that the evidences of a cured phthisis are present, much more frequently than is generally supposed, in the lungs of those who present no signs of the existence of phthisical processes at the time of death. This impression has been confirmed by a study of the carefully recorded reports of 1,146 post-mortem examinations made at the dead-house of Bellevue Hospital. Those reports which were incomplete have not been included in this study. Of these 1,146 autopsies, 383 were made on persons who died either from tuberculosis, or showed in their organs an active or chronic tubercular process. This left 763 autopsies made on non-tubercular subjects; of these, 276, or thirty-six per cent., showed lungs which were bound by organized adhesions, either general or local, to the chest-wall. In all of these 276 cases the lungs were free from disease, except the pleuritic changes which, in most instances, interfered materially with the perfect expansion of the lungs, as the study of microscopical sections made from the underlying pulmonary tissue clearly demonstrated. Of the 763 persons dying of a non-tubercular disease, 71, or over nine per cent., presented in their lungs changes which I regard as characteristic of healed pulmonary tuberculosis. Many writers on phthisis give the percentage of cases of cured phthisis as much lower. For instance, Dr. Williams, of London, out of 1,000 cases in private practice, states a cure was effected in 4.6 per cent.; Dr. Austin Flint, in 640 cases, says a recovery took place in 44, or 6.5 per cent.

These conclusions were reached from physical examinations, and not from post-mortem appearances. When we study tuberculosis from a pathological standpoint, we look more hopefully on the disease as amenable to cure. Vibert,¹ from the register of the necropsies made at the Paris morgue, found in 17 out of 131 persons dying from violence or sudden death the evidences of pulmonary tuberculosis which had been cured. This is a little over twelve per cent., and shows a higher rate of cured phthisis than that obtained by me. Joseph Coats, of Glasgow, reports that out of 103 persons dying of a non-tubercular disease, 20 showed in their lungs the evidences of healed phthisis; this is a little over nineteen per cent. The report of the Middlesex Hospital, compiled by Dr. Fowler, gives the arrest and cure of pulmonary tuberculosis in 177 cases out of 1,943 necropsies which were made by him; this is about nine per cent. Dr. Sidney Martin reported before the British Medical Association that in 445 consecutive post-mortem examinations he had found 42 cases of healed tuberculosis in the lungs, or 9.4 per cent. These 42 persons died of a non-tubercular disease; 7 of them of cancer. This relation between cancer and healed tuberculosis has been observed and commented on by all investigators in this field. As these percentages are much higher than those given by clinical observers it is evident that recovery from phthisis is more frequent than generally supposed. The class of cases examined at the Bellevue dead-house came from the lower walks of life, and during life were under the worst possible hygienic conditions, and yet nine out of every hundred furnished those pulmonary lesions which are evidences of cured phthisis. The question which may naturally be asked is, what are the lesions which are evidence of cured phthisis, and how can one say the disease is cured from the appearances which are found?

If by the term "cured phthisis" is meant a complete restoration of the affected portion of the lungs to a normal condition, we can say that it never occurs; but if it

¹ London Lancet.

is meant that all pulmonary symptoms cease, that the patient has good health, and that the damage to the lungs is not sufficient to prevent an adequate use of their functions, and that the tubercle bacilli, if present, are rendered inert by the connective tissue which surrounds them, and are finally destroyed, then we can say that a cure takes place in very many cases—a number much larger than is generally supposed.

It is impossible to understand how recovery from primary or secondary areas of tubercular infiltration in the lungs can take place by absorption of the tubercular material, and the restoration of the lungs to a perfectly normal condition. If, then, every tuberculosis, although cured, leaves its permanent stamp on the tissues, what are the steps by which an exceedingly destructive process becomes arrested and cured?

In describing these changes, I will speak, 1, of their situation; 2, of their gross appearance; and 3, of their microscopical appearance.

The post-mortem appearances in cases which may be regarded as cured will necessarily vary with the extent of the tuberculosis and the stage to which it had advanced before its arrest. As phthisical processes are usually confined to the apex of the lung, the changes of repair were better marked here than elsewhere, although in a few instances these changes were found in other places, especially the posterior aspect of the lower lobes, and in the lower part of the upper lobe. On the basis of their gross appearance, I shall group my cases under the following heads:

FIRST.—*That class in which the apex of the lung is found adherent to the costal pleura, with a puckered and depressed condition of its surface.* Sixty of the seventy-one cases which form the basis of this paper showed this condition. On cutting into the lung, one or more dense fibro-cartilaginous nodules, varying in size from a cherry to a walnut, are seen beneath the depressed surface, or, if situated in the central portion of the upper lobe, are generally connected with the surface by easily recogniz-

able dense bands of new connective tissue. In the centre of these nodules, a chalky mass is often found, sometimes soft, but generally of sandy consistency, and often studded with sharp spiculæ, as hard as bone.

Photograph 5 shows one of these nodules situated at the apex of the left lung. The puckered appearance about the nodules is due to the contraction of the newly formed connective tissue. The surface of the lung over the nodule was adherent to the costal pleura. The contents of the mass was cheesy, of a dark gray color, and contained no tubercle bacilli. In a few instances, the centre of the mass appears dense and cartilaginous, and the nodule presents the appearance of a solid body.

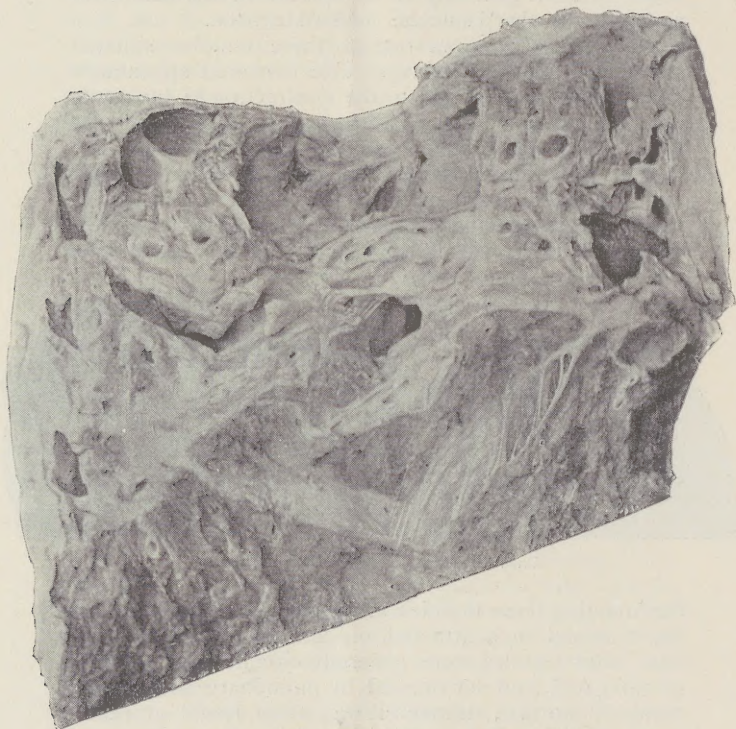


PHOTOGRAPH 5.—Fibrous Nodule at Apex.

Surrounding these nodules are laminated fibrous deposits, traversed by contracted, obliterated, or dilated bronchi. The nodules were generally circumscribed, round, or elongated, and surrounded by pulmonary tissue which appeared normal, although it was often found on examination to be only in part permeable to air, or to be the seat of well-marked emphysema.

In a few cases, the indurated portions of the lungs were not nodular, but diffuse and more extensive, and these were situated, not in the central portions of the lung, but in connection with the pleura. They consisted of dark-gray fibrous tissue, dense, tough, and often very hard, resembling cartilage, and contained no caseous residues,

although generally some were scattered throughout the tissue, and appeared to be derived principally from altered bronchial secretions.



PHOTOGRAPH 4.—Upper Lobe Replaced by Fibrous Tissue.

Photograph 4 shows the substance of the upper lobe of the right lung entirely replaced by new fibrous tissue. The pleura is greatly thickened. The rest of the right and all of the left lung were perfectly normal.

Often all trace of alveoli had disappeared. Connected with the thickened pleura are septa running through the



PHOTOGRAPH 3.—Healed Cavity.

lungs, composed of a condensed cellular substance intermingled with fibrous tissue. These septa from their whiteness form striking contrasts with the rest of the lung.

Photograph 3 shows a healed cavity in an otherwise perfectly normal lung. The wall of the cavity was nearly a quarter of an inch in thickness, and composed of dense, fibrous tissue. The cavity was empty. This is the best illustration of a healed cavity that I have ever seen. The specimen belongs to Dr. T. M. Prudden, who kindly loaned it to me.

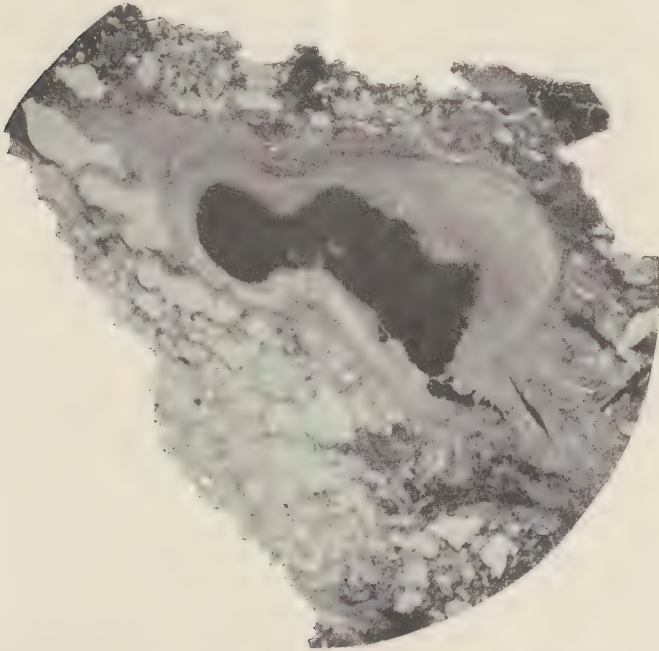
SECOND.—*One of the most positive evidences that phthisis which has gone on to the formation of cavities can be recovered from, is the aspect presented by healed cavities.* Six of my cases showed this condition, and divided themselves into two forms :

1. Where the cavity was empty and communicated with a bronchus. I have met with but two of these cases and both of them were found in the central portion of the lung. The cavities are closed on all sides and lined with a thick, dense fibrous or fibro-cartilaginous membrane, sometimes half an inch in thickness. This forms an internal cicatrix analogous to a fistula. The cavity is kept open by adhesions of the lobe to the chest-wall. Sometimes these cavities are not empty, but partly filled with calcified tubercular material, or a fibro-cartilaginous mass due to vegetations from the wall of the cavity. The surrounding pulmonary tissue is rarely perfectly healthy, generally it is indurated, infiltrated with black pigment, and puckered by shrinking.

2. Most frequently the cavity was contracted to such an extent by the growth of fibrous tissue that it was almost obliterated and appeared as a linear cicatrix. I have often found this connective-tissue over an inch in thickness, surrounding what remained of a cavity.

Photograph 2. This is a photo-micrograph, showing the great increase of connective-tissue about a contracted and almost obliterated cavity. At the lower portion of the photograph new connective tissue could be seen forming in the alveolar walls.

The adjoining pulmonary tissue may appear normal, although, when examined, it is found to be generally the seat of emphysema, and to contain patches of interstitial pneumonia. The condensation and contraction in the pulmonary tissue causes the emphysema, and is, I believe,



PHOTOGRAPH 2.—Photo-micrograph. Contracted Cavity Surrounded by Fibrous Tissue.

essentially connected with the spontaneous cure of pulmonary cavities. Sometimes calcareous concretions, like small, opaque, granular, or chalky deposits, are found in the centre of the cicatrix; these are the contents of the obliterated cavity. (In the young, the calcareous deposit

takes place at the periphery, leaving a calcareous crust with a soft centre.) I found these internal cicatrices almost always accompanied by puckering of the corresponding surface of the lung, with depression of the chest-wall.

THIRD.—*Two cases have come under my observation where there had been a complete transformation of the whole of an upper lobe into a compact homogeneous mass of fibrous tissue, without a vestige of pulmonary substance.* Throughout the lobe were seen large numbers of dilated bronchi, many of them filled with calcareous matter. The whole lobe was impervious to air, uniformly pigmented, of a bluish slate color, and presented none of the gross appearances of a tubercular process. This was only settled by a microscopical examination, which showed giant-cells in large numbers, mingled with tubercular and fibrous tissue. The tissue was scantily supplied with blood-vessels; many of the bronchial veins were obliterated, and the bronchi closed.

Black carbonaceous deposits are apt to take place during the healing process of phthisis, in the neighborhood of (cretaceous) concretions and cicatricial tissue; they may be circumscribed or diffuse, and give the tissue a bluish-black or slaty-gray color. In all lungs showing the changes of healed phthisis at the periphery, and in most of those where the changes are confined to the central portions, one will find the two surfaces of the pleura adherent. A marked depression of the lung was observed in 54 out of 71 of my cases, the surface being hard, uneven, and presenting a crumpled appearance. These depressions depend on the loss of substance of the lung, and the consequent contraction which it has undergone.

Microscopical Appearances.—Normally, in the human lung, there are prolongations of connective tissue passing in from the pleura, and dividing the pulmonary tissue into rounded, polyhedral compartments or lobules. These lobules are in turn made up of a number of primary lobules, composed of a collection of air-sacs or alve-

oli. The prolongations of connective tissue from the pleura or interlobular septa, as they are called, are quite broad, and easily recognizable by the naked eye, for they are usually rendered prominent in the human lung by deposits of inhaled carbon in their lymph-channels. It is this interlobular connective tissue which plays the most important part in the healing of pulmonary tuberculosis.

An examination of microscopical sections presenting the evidences of arrested and healed tubercular processes, has led me to the following conclusions :

All fibrous developments result in induration, but it is not easy to determine how or why the tubercular processes were arrested, or how the final result was brought about.

The indurated portions of the lungs were either in the form of nodular or diffuse masses. In this latter and rarer form, cheesy or calcareous residues were scattered throughout the fibrous tissue. At the edge of the pulmonary tissue, destroyed by the tubercular process, in many sections, new connective tissue could be seen just forming. This seemed to be derived from three sources.

1. The interlobular connective tissue had been infiltrated with round cells which were becoming changed into new connective tissue cells. In some, the interlobular septa had been increased ten-fold, and presented an effective barrier to the advance of the tubercular process.

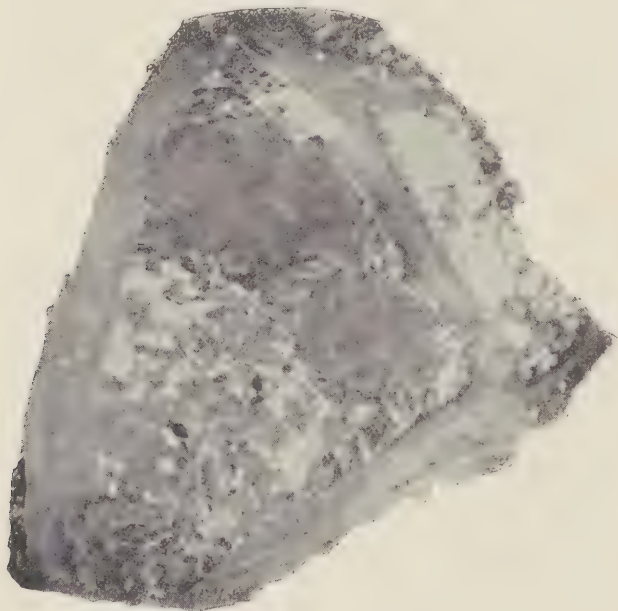
Photograph 1. This is a photo-micrograph showing two broad bands of new connective tissue passing inward from the pleura, completely enclosing a tubercular area, and limiting the extension of the process. The bands are increased interlobular septa.

In all the sections, this interlobular increase was constant and most marked, and in a number seemed to be the primary change. The new connective tissue was highly vascularized.

2. New connective tissue forming in the alveolar walls was seen. In one section adjoining a contracted and encapsulated nodule, the walls of the alveoli presented all the stages of new connective-tissue formation—

round cells elongating and becoming spindle-cells ; spindle-cells changing into dense fibrous tissue ; with, finally, contraction and obliteration of the alveolus and its place taken by new connective fibrous tissue.

I am aware that by many the participation of the



PHOTOGRAPH 1.—Photo-micrograph. Tubercular Area Enclosed by New Connective Tissue.

slight amount of connective tissue in the wall of the alveolus in the general hyperplasia is denied, but it seems to me without question that it does occur.

3. The connective tissue around the vessels and bronchi had become greatly increased. The latter were often almost obliterated by the contractions of the new con-

nective tissue, but I was surprised to see how little the lumen of the pulmonary vessels was interfered with. This was marked in all sections, no matter how extensive the fibrous tissue. In the new tissue, areas of round-cell infiltration were seen, and in places, granules of black pigment occurred in the walls of the bronchi, which were most probably, however, secondary to the fibroid changes. In some sections adhesions of the pleura seemed to be the first step in the development of new connective tissue in the lung substance, for from these adhesions broad bands of new fibrous tissue were almost universally seen dipping deep into the lung. Fibrosis is a conservative process. The new fibrous tissue from the pleura and the interlobular septa offer a dense barrier to the advance of the tuberculosis, and the incipient softening is not attended as is usual by the continued deposition of tubercle. The new connective tissue by its contractions encapsulates the tubercular area, compresses and renders inert the cheesy masses, and limits the advance of cavities, reduces them in size, and finally causes them to cicatrize and entirely disappear.

I could find no evidence, as some claim, that the tubercle itself furnished any of this fibrosis. One fact especially impressed me, and that was the hyperæmic condition of the tissue which surrounded the tubercular areas where the new connection was forming. Throughout the fibrous tissue new capillary vessels were seen everywhere. An unobstructed circulation, and an intense hyperæmia were conditions so constantly present where recent fibroid processes were active that they seem to be essential to the cure of phthisis.

In the fibroid conditions which I have just described, fifteen lungs showing the characteristic lesions of healed phthisis were taken, and a half dozen microscopical sections were cut from each lung. These were stained for tubercle bacilli, and in none were any bacilli found. The sections presented all the microscopical appearances of a healed tubercular process, and I believe the lesions could have been caused by nothing except the tubercle

bacilli. Some would have us believe that these fibroid nodules found at the apex of the lungs are not the result of a tubercular process, but that other irritants besides tubercle may cause them. The burden of proof, it seems to me, must rest with them. Ziegler, who has investigated tuberculosis from its anatomical side possibly more than any other observer, says, in his work on "Pathological Anatomy," that tuberculous lungs may recover locally, and the indurated patches not only contain no tubercle bacilli, but even present none of the special characteristics of tuberculosis.

The following are the reasons why I consider all these nodules of tubercular origin :

1. A number of cases have been reported where the patient was treated ten, fifteen, and even twenty years before death for extensive and well-marked phthisis, from which, after a number of years, they completely recovered, and finally died by accident, or from some non-tubercular disease. At the autopsy, the only pathological change found in the lungs to mark the seat of the old tuberculosis were these characteristic fibrous nodules. Laennec, Bennett, and Jaccoud all cite a number of cases of this kind.

2. It would hardly seem possible that any but a tubercular process could develop fibrous nodules so uniformly at the apex of the lungs.

3. The few nodules which were proven by my inoculation experiments to contain tubercle bacilli, and so beyond question to be tubercular, differed in no respect in gross appearance or anatomically from the other fibrous masses in which no tubercle bacilli were found.

Inoculation Experiments.—These experiments were conducted upon rabbits with the object of ascertaining whether the circumscribed fibrous nodules containing cheesy or chalky deposits, and found generally at the apex of the lungs, contained tubercle bacilli. The settlement of this point is important, for it is the only means we have of ascertaining whether phthisis is ever absolutely cured. Even a few bacilli remaining in an apparently healed

area in the lungs must of necessity always be a source of danger to the individual.

The experiments were conducted in the following manner: The nodule or nodules were laid open by a sterilized knife, the contents removed by sterilized needles, and then dissolved in distilled water in an aseptic vessel. One to two cubic centimetres of this fluid were then injected, under strictly antiseptic precautions, into the right pleural cavity of a healthy rabbit, which was killed in from six to twelve weeks, after being kept under the best hygienic surroundings. A history of the cases from which the nodules were taken and a record of the autopsy on the rabbit were kept. The following is a detailed account of the experiments:

Rabbit No. 1. Inoculated in right pleural cavity with 1 c.c. of fluid obtained by dissolving the cheesy contents of a single nodule, three-eighths of an inch in diameter. The nodule was obtained from the upper portion of the apex of the right lung, which together with the left lung was perfectly normal. The subject from whom the lungs were removed, died suddenly from a rupture of an aneurism of the descending portion of the arch of the aorta. The rabbit was killed at the end of three months, and all its organs were found in a normal condition.

Rabbit No. 2. Inoculated with 1 c.c. of sterilized water in which were dissolved the cheesy contents of two yellowish-white nodules which were surrounded by radiating bands of connective tissue in such a manner as to give the lung about the mass a puckered appearance. The nodules were situated in the centre of the upper lobe of the right lung, and the cheesy centres were one-half and one-fourth of an inch in diameter respectively. The man from whom the lungs were removed died from a blow on the head, which caused a fracture of the parietal and temporal bones, with laceration of the brain-substance. The rabbit was killed at the end of five weeks, and, with the exception of localized adhesion of the lung to the costal pleura at the point where the needle pierced the chest-wall, all the organs were normal.

Rabbit No. 3. Inoculated in the usual way with the cheesy contents of two nodules, each about half an inch in diameter, and situated at the apex of the right lung. The lungs, with all the other organs, were found in a normal condition. The man died suddenly from "Paris-green poisoning." The rabbit was killed in the fifth week after inoculation, and all its organs presented a normal appearance.

Rabbit No. 4. Inoculated with 3 c.c. of fluid obtained by dissolving in sterilized water the soft, cheesy contents of two nodules, one inch, and one-half inch in diameter, respectively. These nodules were situated at the right apex, an inch and a half from the pleura, and were surrounded by well-organized connective-tissue bands. The pulmonary parenchyma for about an inch and a half around these nodules contained twenty gray translucent masses, the size of a pin's head, which looked like miliary tubercles. The smallest bronchi in this area contained pus. With these exceptions, both lungs were perfectly normal. The person from whom they were removed died of chronic Bright's disease. The inoculated rabbit was killed at the end of three months, and in both lungs were found consolidated cheesy masses, the size of a pea, which showed on microscopical examination, the structure of tubercles. The rest of the organs were normal. The contents of the nodules removed from this person, therefore contained tubercle bacilli, and a very recent eruption of miliary tubercles surrounded them, possibly favored by the weak condition of the person two months before death.

Rabbit No. 5. Inoculated with $\frac{1}{2}$ c.c. of fluid obtained from the contents of an old encapsulated nodule three-fourths of an inch in diameter, situated at the apex of the left lung. With this exception, the lungs were perfectly normal. The person died of general abdominal tuberculosis; miliary tubercles studded the omentum, and covered every portion of the small intestines. The nodule in the lung was the only old tubercular process found in the body. Dr. Biggs performed the autopsy.

The rabbit, which had become very much emaciated, was killed on the thirtieth day after inoculation, and milary tubercles were found scattered throughout both lungs. This is a very interesting case, and forcibly impresses the fact of the danger which may lurk in these apparently inert nodules.

Rabbit No. 6. The case from which this rabbit was inoculated was in Bellevue Hospital, under treatment for phthisis. At the autopsy the lungs were found perfectly normal, but there was an aneurism of the arch of the aorta which caused the phthical symptoms. The contents of two nodules situated just beneath the pleura of the right apex, and about three-fourths of an inch in diameter, were injected into the right pleural cavity of a healthy rabbit. The rabbit was killed at the end of six weeks, and all its organs were normal.

Rabbit No. 7. Inoculated with 1 c.c. of a fluid obtained by dissolving the calcareous and cheesy contents of a single large nodule, an inch and a half in diameter, situated near the apex of the right lung. The nodule was surrounded by layers of fibrous tissue, one-fourth of an inch in diameter. The surface of the lung was puckered, and a broad band of new fibrous tissue ran from the nodule to the depressed surface. The patient died from cirrhosis of the liver. The rabbit was killed at the end of eight weeks, and, with the exception of a localized pleurisy, the lungs and all the organs were normal.

Rabbit No. 8. The patient, who died of heart disease, from whom this rabbit was inoculated, had just beneath the pleura in the upper lobe of the right lung a circumscribed fibrous nodule, three-fourths of an inch in diameter. In the substance of the lobe were a number of smaller nodules limited by concentric bands of fibrous tissue. All the nodules had cheesy centres. The contents of the large nodule with that of three of the smaller were dissolved in sterilized water, and 1 c.c. injected into the pleural cavity of a rabbit. The rabbit was killed five weeks after inoculation, and all its organs were normal.

Rabbit No. 9. Inoculated $1\frac{1}{2}$ c.c. of the fluid ob-

tained by dissolving the scraping from the wall of a contracted cavity, one inch in diameter, situated in the centre of the right upper lobe. The cavity was surrounded by fibrous tissue, one-fourth of an inch thick ; it was free from contents, and did not communicate with a bronchus. The patient died of cerebral hemorrhage. In the sixth week the rabbit was killed. The lower lobe of the right lung was bound to the chest-wall ; with this exception the lungs and all the other organs were normal.

Rabbit No. 10. The patient from whom this rabbit was inoculated died from chronic diffuse nephritis, with a large dilated heart, and general arterial disease. The upper lobes of the right lung contained ten nodules, varying in size from that of a dime to a small pea, and all surrounded by a very dense capsule of connective tissue. The contents of most were cheesy. The largest nodule was selected and a rabbit inoculated with 1 c.c. of the fluid obtained from dissolving the contents in sterilized water, with the exception of these nodules, and a very thick pleura over the entire right lung, both lungs were perfectly normal. When the rabbit was killed at the end of two months, about half a dozen small tubercular masses were found in both lungs, showing conclusively that the contents of the largest nodule selected contained tubercle bacilli.

Rabbit No. 11. Inoculated in the usual way with the calcareous and cheesy contents of two nodules, three-fourths and three-eighths of an inch in diameter respectively, situated just beneath the pleura at the apex of the right lung. The greater portion of the contents of the nodules was calcareous. The patient died from a gunshot wound of the abdomen. The rabbit was killed on the fortieth day ; all the organs were normal.

Rabbit No. 12. Inoculated with 2 c.c. of fluid, obtained by dissolving the contents of two small nodules, about half an inch in diameter, situated in the central portion of the upper lobe. These nodules were surrounded by but little fibrous tissue. The patient from whom they

were removed died suddenly of lobar pneumonia. The rabbit was killed on the thirty-fifth day, and with the exception of localized adhesions at the point where the needle entered the chest-cavity, all the organs were in normal condition.

These inoculation experiments show that while in the majority of cases no tubercle bacilli could be demonstrated in the healed pulmonary areas, still the fact that they were found in certain instances where the disease had remained latent for an indefinite period, and the nodules presented the same appearance as in the other cases, emphasized the difficulty of determining just when all dangers from old phthisical processes have ceased. Experiment No. 5 showed that the general abdominal tuberculosis from which the patient died, was due to the escape of the tubercle bacilli from the old and apparently encysted nodule at the apex of the left lung. I can recall a number of cases of miliary tuberculosis, and some of tubercular meningitis, where the only tubercular process which could be found in the body was an encapsulated nodule in the lungs, containing possibly some cheesy material.

These experiments will at least demonstrate the possible dangers which may lurk in these apparently inert masses. Experiments 4 and 10 showed tubercle bacilli in the healed areas in the lungs, and proved that even from these nodules, to all appearances completely enclosed by fibrous tissue, tubercle bacilli had escaped and caused the eruption of miliary tubercles, which were seen about the masses in both cases. Possibly the physical organism had undergone certain changes in these cases. In Case 4 a localized bronchitis was found; in Case 10 the patient with chronic Bright's was very sick for two months before death. Both of these conditions may have favored the escape of the tubercle bacilli.

May we not here have an explanation of the sudden development of the phthisis in those cases where a localized, and perhaps forgotten, tuberculosis from which apparent recovery has been made, suddenly redevelops.

Conclusions.—I offer the following as reasonable conclusions from the foregoing studies. The microscopical examinations seem to establish that fibrosis is the only method by which tuberculosis of the lungs can be recovered from, and although they accord with well-known facts, recognized as long ago as the time of Laennec, by whom the first, and without question best, description of these changes was given, I offer no apology for going over again what may seem at first sight a well-worn subject, for my endeavor has been to study the methods of the formation of this fibrous tissue and the elements from which it is derived. The gross description of the lungs which I have given is the natural grouping of those which have come under my observation.

I have been able to find in medical literature but a few statements as to the percentage of cases of cured phthisis, based on post mortem examinations. In consideration of the large number of cases from which these conclusions are drawn, I believe the time spent in this work has not been in vain.

As to the presence or non-presence of tubercle bacilli in the healed areas, as far as I know this point has never before been investigated. In all the cases examined, and from which I have made inoculation experiments upon rabbits, tubercle bacilli were found in only three instances.

There was one suggestive fact found in my examination, viz., that whenever the nodular mass or masses presenting the anatomical characteristics of healed phthisis were situated in the substance of a lobe, a broad and easily recognized band of new connective tissue passed from the nodule to the pleura through the apparently healthy pulmonary tissue. Sometimes there were more than one of these bands. At the place where the bands reached the surface of the lungs, evidences of a localized pleurisy were found, generally with adhesion of the two surfaces of the pleura. How to explain the presence of these bands is not easy. Its appearance, so often repeated, suggested that some constant and determinable influences were at work, and in the study of the lymphatics

and the distribution of pigment in the lungs rests, I believe, an explanation. After consulting all the writings on the lymphatic circulation of the lungs to which I had access, two conclusions presented themselves: First, that the subject is one which had been but imperfectly investigated, and about which little is known, most anatomists dismissing the matter at short hand; and secondly, that the consensus of opinion, including such writers as Sappey, is, that there are two systems of lymphatics in the lungs, namely, those in and beneath the pleura, which empty into the bronchial glands and are entirely distinct from the others in the lung substance itself, which latter follow the vessels and converge at the root of the lungs where they also empty into the bronchial glands.

To ascertain in what direction from the point of injection inert particles, such as carbon, would be carried when introduced into the lung substance the following experiments were made upon rabbits:

Into the lung-substance, as near the centre of a lobe as possible, four healthy rabbits were injected, under antiseptic precautions, with a fifth of a cubic centimetre of sterilized water. The water injected into two of the rabbits held in suspension powdered charcoal; that injected into the other two, carmine. The rabbits were killed at the end of the third, thirtieth, and fortieth days, and microscopical sections were cut at right angles to the surface of the lungs, extending from the pleura to the root of the lungs.

It became evident that the pigment was carried from the centre of a lobe, where a large mass of it was collected, not only outward to the pleura but inward to the root of the lung—most of the pigment passing in the latter direction.

Pigment-granules were seen along the surface of the pleura only over the central mass of injected pigment, in the interlobular connective tissue, running inward from the pleura, and also in pigmented cells found in the smallest bronchi.

While no doubt some of the pigment in these cases was

carried toward the surface of the lung by the bronchi and blood-vessels, the continuous lines of pigment-granules seen in some of the interlobular connective tissue would point to the lymphatics as being instrumental in diffusing the pigment toward the surface of the lungs, even to the pleura. The interlobular tissue of the lung of the rabbit inoculated with the carbon granules was beautifully mapped out by the pigment.

A study of a number of microscopical sections made of normal lungs, and of lungs in which an old tuberculosis was present, leads me to believe that the lymphatics situated in the interlobular connective tissue run toward the pleura; certainly those at least seem to do so which are situated in the outer third of the lung. The distribution of the pigment noted in these cases seems to help to explain the formation of the characteristic bands of new connective tissue which I found in the human lungs, extending from the nodules located in the central portion to the overlying pleura. In none of the sections was there noted a band extending in any other direction. Inferences might be drawn thus: The inflammatory products resulting from the destruction of tissue by the tubercular processes which have taken place in the central portion of the lungs are carried in the lymphatics which run in the interlobular septa to the pleura. There a localized pleurisy is set up; this may be the first intimation given by physical examination that tuberculosis has commenced. So also the pleuritic crepitation heard must have a special pathological significance, ante-dating often any other physical sign. In like manner, it is readily seen how the interlobular connective tissue irritated by the inflammatory products in the lymphatics increases, and so are formed the broad bands of new tissue which are noted in these cases.

My examinations also show that it is not the tubercle which undergoes healthy evolution, but the normal connective tissue of the lungs, which surrounds it, and of this connective tissue, it is the interlobular, assisted by that of the pleura which first increases, and is able to

resist the advance of the destructive processes. If by any means the vessels in this tissue can be kept open, the capillaries filled with blood, fibrous processes will be established as the result of the irritation, and the active congestion. If there is any virtue in Koch's "tuberculin," high elevation, or certain indirect methods, as the pneumatic cabinet, may it not be due to the localized congestion which they excite? A microscopical examination of the lungs removed from three patients who had been treated for a long time by injections of Koch's "tuberculin," showed a most intense active hyperæmia of all the vessels in and around the old fibroid areas at the apex of the lungs. In these situations an unusual formation of new connective tissue was taking place. The microscopical appearance of these lungs differed in this respect from all others I have ever examined. When once formed, the fibrous growth acts as a bulwark to prevent the irritation and extension of the tubercle bacillus. In this way such tubercular exudation as has occurred will be rendered abortive, and even large ulcerations will be healed and cicatrized by the newly formed connective tissue. In examining the lungs which I removed from a patient who died a few months ago in Bellevue Hospital, I found in the upper lobe of one lung, a cavity the size of a walnut. This cavity communicated with a bronchus, and had a dense fibrous lining, fully one-eighth of an inch in thickness. It was filled with masses of cheesy tubercular material, which contained tubercle bacilli in large numbers. In the upper lobe of the opposite lung was an eruption of miliary tubercles, covering an area about two inches in diameter. A careful examination showed the walls of the cavity to be intact, and that it had resisted the advance of the tubercular process. In one of the larger bronchi was found a tubercular mass covering an ulcerated surface, showing that the infection must have extended from the old cavity by way of the bronchi to the opposite lung. Here lurks another danger of an incompletely healed tubercular process in the lungs, and not till every avenue of exten-

sion is shut off, and the cavity free from tubercular products containing bacilli, can we consider pulmonary tuberculosis as cured. The few encapsulated tubercle bacilli must then be rendered inert. The two healed cavities which I have previously mentioned in my cases were free from any material; their walls were fibrous looking, and contained no vegetations. The contracted cavities, which communicated with no bronchus, contained but little material. Whether this had been removed by expectoration or absorption it is hard to say.

It is a well-known pathological fact that loss of the parenchymatous elements of a tissue or organ is followed by a new growth of connective tissue to take their place. The new growth must be pathological in intensity to be effective when there is much destruction of tissue. May not this rule be applied to the lungs to explain the conservative changes which take place in them? In phthisis the pulmonary parenchyma, being of a higher grade of vitality than the connective tissue, is acted upon and destroyed first by the tubercle bacilli. The surrounding connective tissue is stimulated to increased activity by the irritation which is produced, just as occurs in other places in the body on the application of an irritant. Again, the parenchyma of the lungs being destroyed, the connective tissue must increase to fill the vacancy produced. Laennec and Bennett both describe autopsies made on private patients who had been under observation for a number of years, in whom a careful study of the physical signs indicated that cavities had formed and gradually cicatrized. At the post-mortem, the place of these cavities was entirely taken up by new connective tissue formation, and no collapse of the lungs had occurred to aid their obliteration.

Before closing this article, I would acknowledge my indebtedness to Dr. Henry S. Stearns for the photographs which he has kindly taken for me, both of the gross specimens, and of the microscopical sections.

As a summary, and a partial answer to the question with which this paper opened, I would suggest the following :

1. Out of 763 persons dying of a non-tubercular disease, 71, or over nine per cent., at some time in their life, had phthisis, from which they had recovered.

2. The new fibrous tissue by which the advance of the disease was apparently checked, and the cure effected, developed principally by round-cell infiltration of the interlobular connective tissue, which in some instances had increased to an enormous extent. Some of the new fibrous tissue was formed later by round-cell infiltration in the alveolar walls and around the blood-vessels and bronchi. Pleuritic fibrosis appears to be secondary to tubercular processes in the lung-substance. The interlobular connective tissue is the primary and principal source of the fibrosis.

3. Tubercle bacilli were present in the healed areas in three out of twelve of the lungs examined. These healed areas did not differ in their gross or microscopical appearances from those in which they were not found.

4. Thirty-six per cent. of all cases where the lungs were free from disease showed localized or general adhesions of the two surfaces of the pleura.

